Attorney Docket No.: 085933/0117
Appln. No.: 09/673,836

## REMARKS

## I. INTRODUCTION

Receipt of the Office Action of November 19, 2002, is acknowledged. The specification has been amended to add an abstract. A substitute specification is also submitted herewith which provides headings for the appropriate sections of the specification.

Claim 1 has been amended to positively recite manipulative steps in the conversion process of the echinocandin class of peptides to their deoxy analogues. Claim 2 has also been amended to positively recite a manipulative step in the conversion process.

Claims 1-4 are pending in this application.

Because the foregoing amendments do not introduce new matter, entry thereof by the Examiner is respectfully requested.

## II. THE OFFICE ACTION

The specification was objected to for allegedly failing to contain headings, lacking an abstract, and using trademarks without capitalizing the names. The claims were also rejected under 35 U.S.C. § 112, first and second paragraphs.

### A. Objections to the specification

#### 1. Arrangement of the Specification

The Examiner objected to the specification for failing to contain section headings such as: (a) Title of the Invention; (b) Background of the Invention; (c) Brief summary of the invention, *etc.* To overcome the objection, a substitute specification is submitted herewith including headings in the text of the specification. No new matter has been added to the substitute specification.

#### 2. Abstract

The Examiner stated that the present application fails to contain an abstract. It is respectfully submitted that the corresponding international application contained an abstract. The International Bureau transmits an abstract along with the national stage filing when Applicants enter the United States national stage via a 35 U.S.C. § 371 application. Thus, an abstract should have been provided

to the USPTO by the International Bureau. However, to expedite prosecution in this matter, an abstract is submitted herewith.

3. Use of Trademarks in the Specification

The Examiner objected to the use of "Sephadex" in the specification where it is not capitalized. The application has been amended in response to the Examiner's objection.

B. Rejections based on 35 U.S.C. § 112, first paragraph

Claims 1 and 2 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly based on a non-enabling disclosure. Applicants respectfully traverse.

The Examiner states that the claims are based on a disclosure which is not enabling. Contrary to this assertion, Applicants' specification provide details regarding how to perform the claimed process. In addition, the disclosure provides an example, which involves the conversion of mulundocandin to deoxymulundocandin by selective reduction. One skilled in the field of organic chemistry would be able to perform a selective reduction of an echinocandin peptide given Applicants' teachings.

Thus, the present specification clearly enables one skilled in the art to practice the claimed invention of converting echinocandin peptides to their deoxy analogues based on the description and examples in the specification.

Without acquiescing to the propriety of the rejection, claims 1 and 2 have been amended to positively recite the method steps necessary for carrying out the conversion by selective reduction.

Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

C. Rejection based on 35 U.S.C. § 112, second paragraph

Claims 1-4 were rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite. Applicants respectfully traverse.

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The Examiner states that claims 1-4 are indefinite because the claims fail to recite method steps for the process of converting echinocandin peptides of formula I to their deoxy analogues. In particular, the Examiner asserts that the claims must positively recite the conversion process steps.

Without acquiescing to the propriety of the rejection, claims 1 and 2 have been amended to positively recite the steps necessary for carrying out the conversion by selective reduction.

Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

## III. CONCLUSION

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

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**Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees; and applicant(s) hereby petition for any needed extension of time.**

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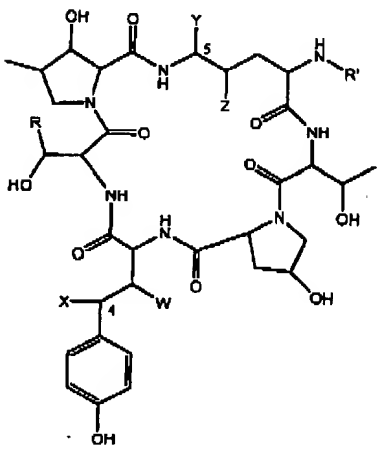
## VERSION WITH MARKINGS TO SHOW CHANGES MADE

**IN THE SPECIFICATION:**

Br fractionation using normal phase chromatography (using alumina or silica gel as stationary phase and eluents such as petroleum ether, ethyl acetate, dichloromethane, chloroform, methanol or combinations thereof), reverse phase chromatography (using reverse silica gel like dimethyloctadecylsilylsilica gel, also called RP-18 or dimethyloctylsilylsilica gel also called RP-8 as stationary phase and eluents such as water, buffers such as phosphate, acetate, citrate (pH 2-8) and organic solvents such as methanol, acetonitrile, acetone, terahydrofuran or combination of solvents), gel permeation chromatography – using resins such as [**"Sephadex LH-20®"**] SEPHADEX LH-20® (Pharmacia Chemical Industries, Sweden), TSKgel Toyopearl HW (TosoHaas, Tosoh Corporation, Japan), in solvents such as methanol, chloroform or ethyl acetate or their combination or [**Sephadex G-10 and G-25**] SEPHADEX G-10® and SEPHADEX G-25® in water ; or by counter-current chromatography using a biphasic eluent system made up of two ore more solvents such as water, methanol, ethanol,. *iso*-propanol, *n*-propanol, tetrahydrofuran, acetone, acetonitrile, methylene chloride, chloroform, ethylacetate, petroleum ether, benzene and toluene. These techniques may be used repeatedly or a combination of the different techniques may used. Counter-current chromatography (liquid-liquid chromatography) using a biphasic eluent system ITO coil is preferred for purification of the compounds of the invention.

**IN THE CLAIMS:**

1. (Amended) A process for **[the conversion of]** <u>converting</u> echinocandin class of peptides of the formula I:



wherein W, X, Y, Z, R and R' are as defined below:

| | W | X | Y | Z | R | R' |
|---|---|---|---|---|---|---|
| 1. Echinocandin B | OH | OH | OH | OH | $CH_3$ | Linoleoyl |
| 2. Pneumocandin $A_0$ | OH | OH | OH | OH | $CH_2$-CO-$NH_2$ | 10, 12-Dimethyl-myristoyl |
| 3. Pneumocandin $A_1$ | H | OH | OH | OH | $CH_2$-CO-$NH_2$ | " |
| 4. Pneumocandin $A_2$ | OH | OH | H | H | $CH_2$-CO-$NH_2$ | " |
| 5. Pneumocandin $B_0$ | OH | OH | OH | OH | $CH_2$-CO-$NH_2$ | " |
| 6. Pneumocandin $B_2$ | OH | OH | H | H | $CH_2$-CO-$NH_2$ | " |
| 7. Pneumocandin $C_0$ | OH | OH | OH | OH | $CH_2$-CO-$NH_2$ | " |
| 8. Mulundocandin | OH | OH | OH | OH | H | 12-Methyl-tetradecanoyl |

to their C4-homotyrosine monodeoxyanalogues of the formula I, wherein W, X, Y, Z, R and R' are as defined herein below:

| | W | X | Y | Z | R | R' |
|---|---|---|---|---|---|---|
| 1. Deoxyechinocandin B (Echinocandin C) | OH | H | OH | OH | $CH_3$ | Linoleoyl |

| | | | | | | |
|---|---|---|---|---|---|---|
| 2. Deoxypneumocandin $A_0$ | OH | H | OH | OH | $CH_2$-CO-$NH_2$ | 10, 12-Dimethyl-myristoyl |
| 3. Deoxypneumocandin $A_1$ | H | H | OH | OH | $CH_2$-CO-$NH_2$ | " |
| 4. Deoxypneumocandin $A_2$ | OH | H | H | H | $CH_2$-CO-$NH_2$ | " |
| 5. Deoxypneumocandin $B_0$ | OH | H | OH | OH | $CH_2$-CO-$NH_2$ | " |
| 6. Deoxypneumocandin $B_2$ | OH | H | H | H | $CH_2$-CO-$NH_2$ | " |
| 7. Deoxypneumocandin $C_0$ | OH | H | OH | OH | $CH_2$-CO-$NH_2$ | " |
| 8. Deoxymulundocandin | OH | H | OH | OH | H | 12-Methyl-tetradecanoyl |

**[which consists of a single step selective reduction of]** comprising reducing the C4-htyr (homotyrosine) hydroxyl group of echinocandins to their monodeoxy analogues by mixing the echinocandin class of peptides with Raney Nickel in a solvent selected from the group consisting of methanl, ethanol and dioxane at a pH of 3-9 **[under neutral conditions]** without **[prior protection/deprotection of]** protecting and then deprotecting the **[equally facile]** C5-Orn (ornithine) hydroxyl group prior to reducing the echinocandin class of peptides and **[purification of ]** then purifying the monodeoxy compound from the crude reaction mixture.

2. (Amended) A process as claimed in claim 1, comprising reducing **[wherein]** Mulundocandin **[is converted]** to Deoxymulundocandin.

3. (Twice Amended) A process as claimed in claim 1, wherein **[the reduction reaction]** reducing the C4-htyr (homotyrosine) hydroxyl group of echinocandins is carried out by hydrogenolysis with Raney nickel in ethanol at pH 7 and at room temperature.